Urinary Bladder Background Findings in Beagle Dogs: Detrusor Myopathy Remains an Infrequent but Important Finding

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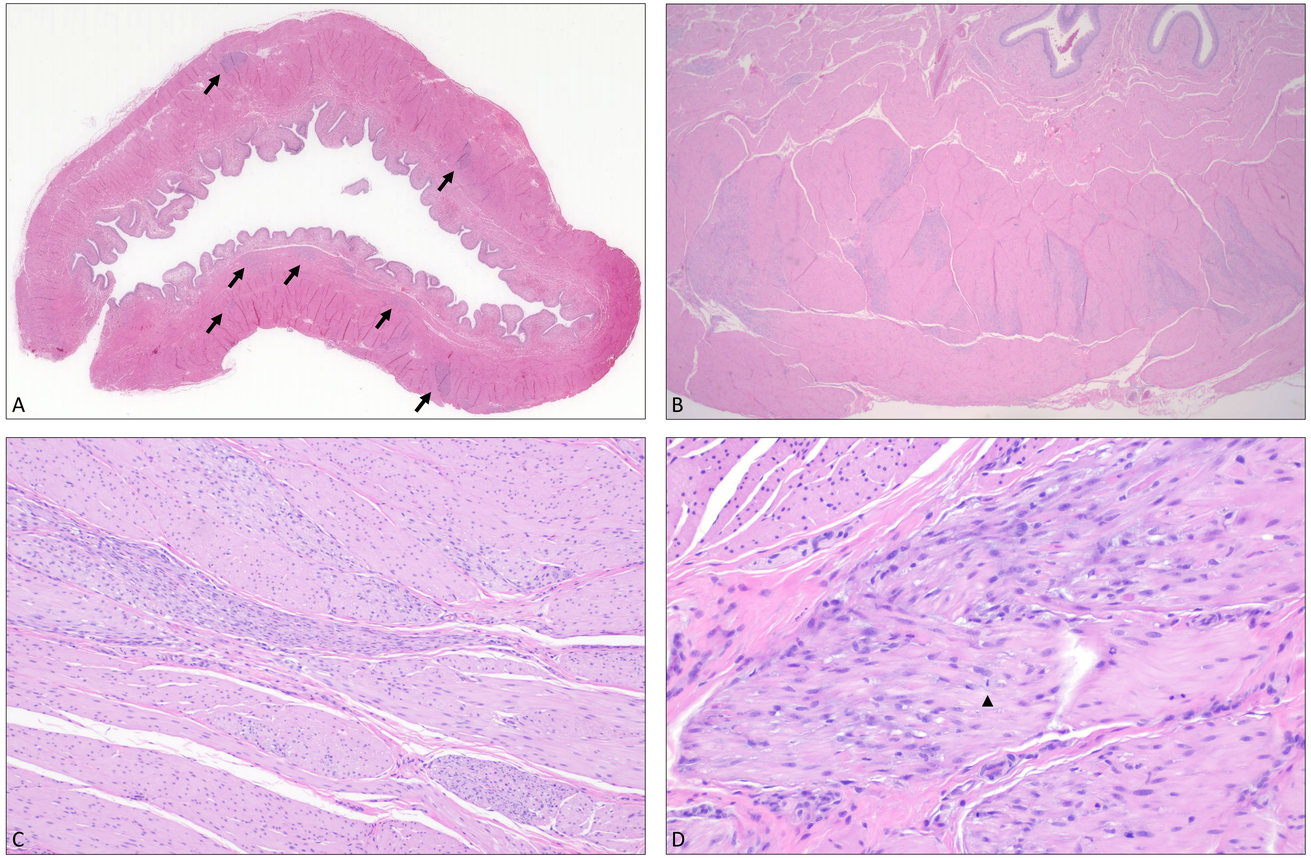
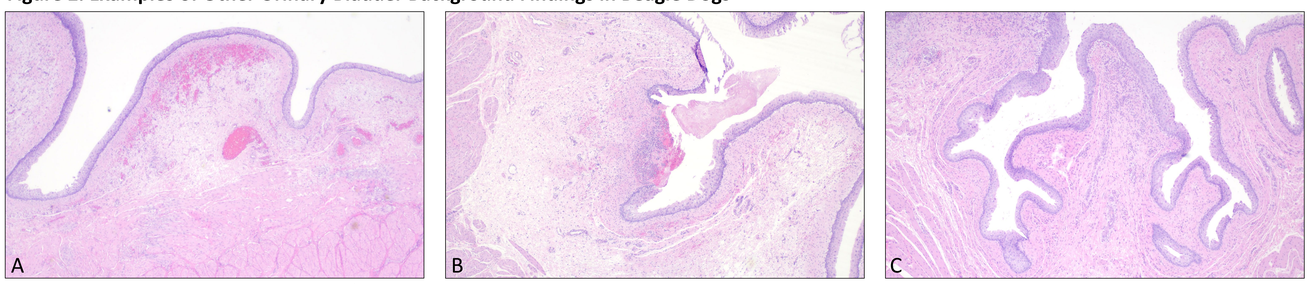
Figure 1. Representative Images of Urinary Bladder Detrusor Myopathy in Beagle Dogs



Urinary bladder detrusor myopathy characterized by multifocal smooth muscle degeneration/regeneration in four dogs: A) small basophilic foci (smooth muscle degeneration/regeneration; arrows) were distributed throughout the muscular tunic (subgross, mild grade), B) at higher severity, basophilic foci (smooth muscle degeneration/regeneration) were larger to coalescing (20x, moderate grade), C) degeneration/regeneration involved muscle bundles to varying degree (100x, mild grade), and D) affected smooth muscles had prominent basophilic, rarely mitotic (arrowhead), regenerative myofibers and intermixed few brightly eosinophilic, occasionally fragmented, degenerate myofibers (200x).

Figure 2. Examples of Other Urinary Bladder Background Findings in Beagle Dogs



Other background findings in historical control and/or contemporaneous studies were uncommon, minor, and not correlated to myopathy. Such findings included: A) minimal hemorrhage within the subepithelial stroma, B) focal ulcer with luminal fibrin aggregate, and C) minimal mononuclear inflammation (40x).

Introduction

Microscopic assessment of the urinary bladder is a standard component of genitourinary system evaluation in non-clinical toxicologic studies. Urinary bladder lesions are uncommon background findings in pre-clinical studies, with lymphoid infiltrates, umbilical remnants, and urothelial vacuolation as examples (Sato et al. 2012, Scudmore 2012). Degeneration of the smooth muscle tunic of the urinary bladder, termed detrusor myopathy, was previously reported in young beagle dogs (Cain et al. 2000), at an incidence of 13% in 449 dogs, no sex predilection, and a possible association to prior catheterization and/or (peri)arteritis. The myopathic lesions within the muscular tunic are described to encompass a spectrum of multifocal morphologic findings indicative of smooth muscle degeneration/regeneration (Woicke et al. 2021). Following observation of lesions consistent with detrusor myopathy of beagle dogs as a notable background finding in a preclinical study, a review of historical control data and contemporaneous studies was performed.

Methods

For historical control data, microscopic urinary bladder findings were compiled for control animals in recent finalized studies (Nov 2022-Dec 2024). For contemporaneous non-finalized studies, urinary bladder slides and urinalysis data from all animals were reviewed. Protocols were also reviewed for variables including animal source, age, naïve status, study design, and urine collection methods. Slides were screened by individual pathologists and lesions were graded by consensus approach of at least three pathologists. Severity grading was based on number, distribution, and size of foci: minimal, few (<5) and small foci (typically less than half of fiber bundle diameter); mild, several (5-10) and/or larger foci (typically half to full fiber bundle diameter); moderate, multiple larger foci to coalescing regions, widely distributed, approximating 25-50% of muscularis affected; marked (>50% of muscularis affected).

Results

Historical control data comprised 87 dogs (44 male, 43 female) from 12 studies, most conducted according to good laboratory practices (GLP, 11/12), with duration 2-39 weeks. Historical control findings consisted of single occurrences of minimal hemorrhage (one female), minimal fibroplasia (one female), and minimal arterial mineralization (one male). There were no recorded muscle findings in historical control records.

Contemporaneous studies encompassed 211 single-source, naïve dogs across 6 studies (4 GLP, 2 non-GLP) at two test facilities with study duration ranging from 3 to 301 days. Five of the studies were initiated within a six-month period. Dogs were 5-11 months of age at study start. Multifocal degeneration/regeneration of bladder smooth muscle occurred in 10 (4.7%) dogs, all males. Lesions were minimal (6), mild (3), and moderate (1) severity, with no relationship to test article administration. Lesions were scattered at all levels of the muscular tunic. Most lesions (9/10) were associated with a test site practicing catheterization for urine collection. There were no associated microscopic vascular findings. There were no consistent urinalysis findings; in particular, positive urine occult blood (semiquantitative dipstick heme pad) results occurred sporadically in animals with and without myopathy lesions, and animals with myopathy had negative results in half of concurrent urinalyses. Other microscopic urinary bladder findings (minimal to mild hemorrhage, edema, inflammation, and/or focal ulcer) were rare (1-2%) and not associated with myopathy, occurring at equivalent or higher incidence in animals without myopathy; ulcer was not identified concomitant to myopathy in any animal.

Conclusions

- Urinary bladder findings were rare in historical background data.
- Detrusor myopathy occurred at low incidence in male dogs primarily in association with routine catheterization.
- No vascular lesions were detected in relation to myopathy.
- Urinalysis showed no specific myopathy-associated findings.
- Other minor background lesions (e.g., hemorrhage, inflammation, ulcer) showed no correlation to myopathy.

Impact

- Detrusor myopathy remains an enigmatic and infrequent but important background finding in dogs.
- Consideration of the method of urine collection is important in contextualizing both anatomic and clinical pathology findings.

References

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